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EVALUATION OF THE CORRELATION OF GLYCOSYLATED HAEMOGLOBIN WITH CENTRAL CORNEAL THICKNESS AND INTRAOCULAR PRESSURE IN TYPE 2 DIABETES PATIENTS

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ABSTRACT

Purpose: To evaluate the correlation of glycosylated haemoglobin (HbA1c) with central corneal thickness (CCT) and intraocular pressure (IOP) in type 2 Diabetes Mellitus (DM) patients. **METHODS**: Values were obtained from 85 healthy control subjects (Group 1) and 85 subjects with type 2 DM (Group 2) with similar age and sex. Cases were further divided into two groups: Group 2A, diabetes patients with HbA1c <7%; and Group 2B, diabetes patients with HbA1c ≥7%. IOP measurements were obtained using Non Contact Tonometer (NCT). Ultrasound Pachymetry was used to measure CCT and corneal-compensated intraocular pressure (IOPcc). **Results:** There was statistically significant difference between Groups 1 and 2 in terms of CCT (p=0.003), IOP (p=0.000) and IOPcc (p=0.018). CCT, IOP, IOPcc were statistically significant between Group 1 and 2B (p=0.002, p=0.000, p=0.037) but not between other groups. **Conclusion:** Type 2 DM subjects were found to have raised CCT, IOP and IOPcc as compared to controls; of which subjects with HbA1c ≥ 7%(Group 2B) were maximally affected which indicates a positive correlation of HbA1c with CCT and IOP.

KEYWORDS: Type 2 Diabetes Mellitus, HbA1c, Central Corneal Thickness, Intraocular Pressure, Corneal-Compensated Intraocular Pressure.

INTRODUCTION

Diabetes mellitus (DM) is a systemic disease that alters the major metabolic pathway in the human body and destroys major organ systems. Type 2 DM is the commonest form of diabetes and constitutes nearly about 90% of the diabetic population in any country. In a diabetic patient, visible lesions take years to develop. However, functional abnormalities may be detected long before anatomical changes are evident. Very early in the disease an increased permeability of the capillary endothelium to plasma proteins is found.[1] Like the vascular endothelium, the function of corneal endothelium is to act as a cellular barrier. If corneal endothelial function is compromised, corneal hydration and consequently the corneal thickness will increase.[2] The range of intraocular pressure (IOP), among the general population, varies from 8-22 mmHg.[3] This variation can be explained by the numerous factors affecting IOP. Previous studies have shown that the factors associated with elevated IOP include smoking,[4] older age,[5] gender,[4,5] blood pressure,[4–6] family history of glaucoma,[4,5] pulse rate,[4,5] diabetes (elevated glycosylated hemoglobin),[4,5] myopia,[7] alcohol usage,[4] race (African),[6] nuclear sclerosis,[5,7] body mass index (BMI)[4–6] and iris color.[7] In this study we aimed to evaluate the correlation of HbA1c with central corneal thickness as well as intraocular pressure.

MATERIALS AND METHODS

This study included the study group (diabetic eyes) and healthy controls. All the patients diagnosed with diabetes mellitus as per ADA criteria 2015[8] were considered for the study. A total of 170 subjects were included in the study. 85 were included in the type 2 diabetes group (group 2) and 85 were included in the control group (group 1) i.e. individuals without diabetes. The cases were further subdivided into two groups: Group 2A, diabetes patients with HbA1c <7%; and Group 2B, diabetes patients with HbA1c ≥7%. Of Group 2, 76.47% belonged to Group2B (HbA1c ≥7%) and 23.53% to Group 2A (HbA1c <7%). Patients with intraocular inflammation, present active eye infection, corneal opacity & scarring, corneal dystrophies and degenerations, history of glaucoma, ophthalmic surgery, ocular trauma, contact lens wear, laser treatment, using topical ocular medications, diagnosed patients of hypertension, proliferative diabetic retinopathy were excluded. Both eyes of each patient were evaluated separately, and anterior as well as posterior segment examinations were included. The average of the readings from both the eyes was taken. According to the principle

of the Declaration of Helsinki, the study was explained to the subjects and they were asked to sign a written informed consent. The research was approved by local ethics committee.

HbA1c is the product of a stable linkage of glucose to the N-terminal valine of the beta-chain of haemoglobin. It defines the average blood glucose level of the previous 2–3 months and reflects the success of diabetes therapy. Thus, it is possible to assess the glucose metabolism of the body more objectively and in long-term than with a blood glucose sample, which reflects only the current sugar level. Usually 4–6.4% of haemoglobin is glycosylated. Higher values are a sign of insufficient blood glucose control.[9] An HbA1c target of <7% for the treatment of diabetes is generally accepted to lower the risk of long term micro or macrovascular diabetes complications.[10] For this reason, patients with type 2 DM were divided into 2 groups according to their HbA1c levels. HbA1c was measured by NycoCard HbA1c kit. It is a boronate affinity assay.

Central corneal thickness was taken from a seated patient by ultrasound pachymetry (Huvitz Pachymetry SP-1000AP by Huvitz Building 689-3, Geumjeong-Dong, Gunpo- Si, Gyeonggi-Do, 435-862, Republic of Korea). Mean of 5 readings was taken. IOPcc estimation was done using the same machine.

Intra ocular pressure was assessed by using non contact tonometer (Huvitz HNT-7000 by Huvitz Building 689-3, Geumjeong-Dong, Gunpo-Si, Gyeonggi-Do, 435-862, Republic of Korea). Mean of 3 readings was taken.

All the measurements were taken in the morning (between the hours of 9:50 am to 10:20 am) and by the same physician.

Statistical Analysis

Statistical analysis were performed by using International Business Machines (IBM) Statistical Product and Service Solutions software version 17(SPSS Inc, Chicago, IL). Sex distribution between the groups was investigated by a chi-square test. The distribution of age and HbA1c values were evaluated by one-way ANOVA. The group including all DM patients (Group 2A and Group 2B) and control group (Group 1) were compared with independent-samples *t*-test. The differences in terms of other variables (CCT, IOP, IOPcc) between groups were evaluated by one-way multivariate analysis of variance (MANOVA). Tukey's multiple comparison test was performed to compare two groups at the same time. The level of significance was set to $p<0.05$.

RESULTS

The three groups were not significantly different in terms of age and sex (Table 2, Table 4) distribution (for age p = 0.973, for sex p=0.361) mean age among the controls was 57.96 ± 11.59yrs and among the cases was 57.88 ± 10.10yrs (Table 1).The mean age was 57.96 ± 11.59yrs, 58.40 ± 8.17yrs and 58.38 ± 13.01 yrs in group 1, 2A, 2B respectively (Table 3).

The mean HbA1c among the controls was 5.83 ± 0.42% and among the cases was 8.93 ± 2.22% (p <0.001,statistically significant ,Table 1). The mean HbA1c among the groups 1, 2A and 2B was 5.83 ± 0.42%, 6.65 ± 0.25% and 9.63 ± 2.08% (p<0.001,statistically significant ,Table 3).

The mean CCT among the controls was 523.72 ± 32.62µm and among the cases was 538.35 ± 30.08µm with a difference of 14.63 µm which was statistically significant (p = 0.003, Table 1). The mean CCT was 523.72 ± 32.62µm, 527.05 ± 26.46µm and 541.83 ± 30.45 µm for groups 1, 2A, 2B respectively. Mean CCT difference was statistically significant between Group1 and 2B (p=0.002) but not between Groups1 and 2A (p=0.950) and Groups 2A and 2B (p=0.122), indicating a significant increase of 18.11µm in CCT in the diabetes group with poor metabolic control (Table 3).

The mean IOP among the controls was 11.97 ± 2.94mm Hg and among the cases was 14.11 ± 3.66mm Hg with a difference of 2.14 mm Hg (p <0.001, statistically significant, Table 1). The mean IOP was 11.97 ± 2.94 mm Hg, 12.68 ± 3.42mm Hg and 14.55 ± 3.64 mm Hg for groups 1, 2A, 2B respectively. Mean IOP difference was statistically significant between Groups 1 and 2B (p=0.000) but not between Groups 1 and 2A (p=0.787) and Groups 2A and 2B (p=0.120), indicating a significant increase in IOP of 2.58 mm Hg in the diabetes group with poor metabolic control (Table 3).

The mean IOPcc among the controls was 13.47 ± 2.73 mm Hg and among the cases was 14.58 ± 3.30 mm Hg with a difference of 1.11mm Hg (p =0.018, statistically significant, Table 1). The mean IOPcc was 13.47 ± 2.73mm Hg, 13.93 ± 2.93 mm Hg and 14.77 ± 3.40mm Hg for groups 1, 2A, 2B respectively. The mean IOPcc difference was statistically significant between Groups 1 and 2B (p=0.037) but was insignificant between Groups 1 and 2A (p=0.890) and Groups 2A and 2B (p=0.638), indicating a significant increase in IOPcc of 1.3mm Hg in the diabetes group with poor metabolic control (Table 3).

Table. 1: Comparison between the cases and controls in terms of various parameters.

	CONTROLS		CASES		P-VALUE
	MEAN	SD	MEAN	SD	
Age	57.96	11.59	57.88	10.10	0.961
HbA1c (%)	5.83	0.42	8.93	2.22	0.000
OD CCT (µm)	523.86	33.14	538.19	31.61	0.004
OS CCT (µm)	523.59	33.08	538.52	29.31	0.002
OD IOP (mm Hg)	11.80	2.86	14.00	3.72	0.000
OS IOP (mm Hg)	12.14	3.28	14.22	3.84	0.000
OD IOPcc (mm Hg)	13.30	2.76	14.42	3.34	0.019
OS IOPcc (mm Hg)	13.63	3.02	14.74	3.53	0.029
Avg CCT	523.72	32.62	538.35	30.08	0.003
Avg IOP	11.97	2.94	14.11	3.66	0.000
Avg IOPcc	13.47	2.73	14.58	3.30	0.018

Notes: The distribution of age and HbA1c values were evaluated by one-way ANOVA. Rest of the parameters were compared with independent-samples *t*-test. **Abbreviations**: SD-standard deviation, HbA1c-glycosylated haemoglobin, OD-oculus dexter (right eye), OS-oculus sinister (left eye), CCT-central corneal thickness, IOPintraocular pressure, IOPcc-corneal compensated intraocular pressure, Avg-average, ANOVA-analysis of variance.

Table. 2: Sex distribution between the two groups.

GROUP	Gender		Total	P-VALUE
	F	M		
CONTROLS	46	39	85	0.110
CASES	37	48	85	
Total	83	87	170	

Notes: The distribution of sex was evaluated by Chi-square test.

Abbreviations: F-female, M-male.

Table. 3: Comparison among the three groups in terms of various parameters.

	GROUP 1		GROUP 2A		GROUP 2B		1/2A/2B	1/2A	2A/2B	1/2B
	MEAN	SD	MEAN	SD	MEAN	SD	P-VALUE	P-VALUE	P-VALUE	P-VALUE
Age	61.34	12.18	58.40	8.17	57.72	10.68	0.132	0.486	0.987	0.156
HbA1c (%)	5.83	0.42	6.65	0.25	9.63	2.08	0.000	0.000	0.000	0.000
OD CCT (µm)	523.86	33.14	527.35	26.48	541.52	32.48	0.004	0.944	0.156	0.004
OS CCT (µm)	523.59	33.08	526.75	27.50	542.14	29.09	0.001	0.961	0.110	0.001
OD IOP (mm Hg)	11.80	2.86	12.65	3.18	14.42	3.79	0.000	0.632	0.130	0.000
OS IOP (mm Hg)	12.14	3.28	12.70	3.89	14.69	3.73	0.000	0.913	0.149	0.000
OD IOPcc (mm Hg)	13.30	2.76	13.91	2.65	14.57	3.52	0.044	0.752	0.749	0.053
OS IOPcc (mm Hg)	13.63	3.02	13.96	3.45	14.97	3.54	0.045	0.972	0.597	0.046
Avg CCT	523.72	32.62	527.05	26.46	541.83	30.45	0.002	0.950	0.122	0.002
Avg IOP	11.97	2.94	12.68	3.42	14.55	3.64	0.000	0.787	0.120	0.000
Avg IOPcc	13.47	2.73	13.93	2.93	14.77	3.40	0.034	0.890	0.638	0.037

Notes: The distribution of age and HbA1c values were evaluated by one-way ANOVA. Rest of the parameters were compared by MANOVA. Group 1 (control group); Group 2A (diabetes patients with HbA1c <7%); Group 2B (diabetes patients with HbA1c ≥7%).

Abbreviations: SD-standard deviation, HbA1c-glycosylated haemoglobin, OD-oculus dexter (right eye), OS-oculus sinister (left eye), CCT-central corneal thickness, IOPintraocular pressure, IOPcc-corneal compensated intraocular pressure, Avg-average, ANOVA-analysis of variance, MANOVA-multivariate analysis of variance.

Table. 4: Sex distribution among the three groups.

	GROUP			Total	P-VALUE
Gender	1	2A	2B		
F	46	8	29	83	0.361
M	39	12	36	87	
Total	85	20	65	170	

Notes: The distribution of sex was evaluated by Chi-square test.

Abbreviations: F-female, M-male

DISCUSSION

On comparing the results of diabetes patients with good metabolic control (Group 2A) and healthy control subjects, there was no significant difference in the value of CCT, IOP and IOPcc. So there is no change of CCT, IOP and IOPcc in the well-regulated DM patient group.

When the DM groups were compared with each other, in Group 2B there was no significant increase in values of CCT, IOP and IOPcc in comparison to Group 2A. When Group 1 and Group2B were compared, significant increase occurred with regard to CCT,IOP and IOPcc in favor of Group 2B indicating a positive correlation with HbA1c. Several studies conducted with specular microscopy show that the corneal endothelium of DM patients when compared with healthy individuals consists of some morphological changes.[11] McNamara et al have reported that hyperglycemia disrupts corneal structure, impairing corneal hydration and therefore affecting corneal thickness in diabetes patients.[12] In the study by Schultz et al barrier and pump function of the corneal endothelium were studied with fluorometric methods and some inability was identified. As a result, changes in corneal thickness in patients with DM has been claimed.[11] According to the results of the experimental study of Herse, the measured decrease in diabetic rabbit endothelial homogenate Na+/K+ ATPase activity strongly suggests that endothelial fluid pump dysfunction is a major component in the abnormal corneal hydration system found in the uncontrolled diabetic rabbit.[13] Most of the studies emphasized that the thickness of the cornea increases with diabetes owing to the disruption of endothelial pump function.[14–16]

The biologic basis of corneal changes in the eyes of diabetic patients has not yet been established and the underlying mechanisms are still unknown. Although CCT changes associated with DM have been reported in various studies and there are different pathogenetic hypotheses, any strong associations have not been established so far between HbA1c and CCT.[14,15,17–21] In the study by Yazgan *et al.*, the biomechanical properties of the cornea in DM patients were found to be deteriorated; however the HbA1c levels were not closely related to deterioration of the corneal biomechanical properties.[22]

Changes in the trabecular meshwork i.e. accumulation of fibronectin, lead to increased IOP.[23] It is possible that the disease diabetes, by activating an unknown mechanism, disrupts the viscoelastic properties of the cornea in the early period and in advanced stages leads to an increase in IOP. Mechanisms, such as degradation mechanisms that facilitate the flow of intraocular fluid or hyperosmolar state due to increased glucose in the anterior chamber may be responsible for higher IOP in patients with poorly regulated diabetes.[22]

The gold standard for the measurement of IOP is the Goldmann applanation tonometer. However, IOP by noncontact tonometer is very popular and widely used for routine ocular examination and correlates well with the Goldmann applanation tonometer. Moreover it has the advantages of not causing abrasion to the cornea, being free from reactions to topical anaesthetics and from spread of infection. Thus, we reviewed the IOP data from those patients who were examined routinely with a noncontact tonometer. The mean IOP among diabetics in our study was lower than other studies.[4,24] When compared to other races, the IOP in the Asian ethnicity is lower.[25] Earlier studies have reported a similar relationship between CCT and IOP among subjects with diabetes.[26,27] A positive correlation of HbA1c with IOP has also been reported.[22]

When Group 1 and Group2B (poor metabolic control) were compared, significant increases occurred with regard to IOPcc in favor of Group 2B. Recent studies have shown that the IOPcc is not affected by corneal properties and thus it provides true measurement of IOP. And yet, these studies argue that IOPcc is a powerful alternative to Goldmann applanation tonometry measurement.[28,29] If the accuracy of this assumption is accepted, this study can draw the following conclusion: In the poorly regulated diabetes patients, IOP is elevated independently from CCT. Also, the GAT gives an accurate intraocular pressure reading for an eye with average CCT, but tends to underestimate or overestimate the true intraocular pressure for thinner and thicker cornea, respectively.[26] Also glycation-induced corneal collagen cross-links in diabetes can cause corneal stiffening, which has also been shown to increase the value of the measured IOP over the true IOP.[30] Hence corneal-compensated IOP (IOPcc) values were taken.

All these parameters were closely related to HbA1c levels. In larger population groups, increased CCT may alarm the observer towards poorly controlled diabetes with raised HbA1c levels. Also HbA1c levels should be done for predictable surgical outcomes Though IOP values showed an increase of 2.58mm Hg in poorly regulated diabetics as compared to controls, IOPcc showed only an increase of 1.3 mm Hg. From this study, it can be speculated that when greater CCT values are considered, the true IOP may possibly be lower in diabetic patients. This interpretation might explain why diabetic eyes tend to have higher IOP values in large population-based studies and why those with diabetes and ocular hypertension have a reduced risk for glaucoma progression.[30]

So, the possibility of a thick cornea should be taken into consideration while obtaining IOP measurements in a diabetic patient. Although present study is done with non contact tonometer, after taking IOPcc, values can be comparable with GAT. In our study, the findings were cross-sectional and we found a positive correlation between HbA1c and mean CCT, IOP as well as IOPcc. In future, a cohort study may be undertaken in which subjects have repeated estimation of all these parameters to reveal the exact relationship between these and HbA1c.

REFERENCES

1. Parving H-H, Noer I, Deckert T, Evrin P-E, Nielsen SL, Lyngsøe J, et al. The effect of metabolic regulation on microvascular permeability to small and large molecules in short-term juvenile diabetics. Diabetologia, 1976; 12: 161–6.
2. Mishima S, Hedbys BO. Measurement of corneal thickness with the Haag-Streit pachometer. Arch Ophthalmol Chic Ill, 1960, 1968; 80: 710–3.
3. Vijaya L, George R, Baskaran M, Arvind H, Raju P, Ramesh SV, et al. Prevalence of primary open-angle glaucoma in an urban south Indian population and comparison with a rural population. The Chennai Glaucoma Study. Ophthalmology, 2008; 115: 648–54.e1.
4. Wu SY, Leske MC. Associations with intraocular pressure in the Barbados Eye Study. Arch Ophthalmol Chic Ill 1960, 1997; 115: 1572–6.
5. Klein BE, Klein R, Linton KL. Intraocular pressure in an American community. The Beaver Dam Eye Study. Invest Ophthalmol Vis Sci., 1992; 33: 2224–8.
6. Bulpitt CJ, Hodes C, Everitt MG. Intraocular pressure and systemic blood pressure in the elderly. Br J Ophthalmol, 1975; 59: 717–20.
7. Weih LM, Mukesh BN, McCarty CA, Taylor HR. Association of demographic, familial, medical, and ocular factors with intraocular pressure. Arch Ophthalmol Chic Ill 1960 2001; 119: 875–80.
8. Association AD. 2. Classification and Diagnosis of Diabetes. Diabetes Care 2015; 38: S8–16.
9. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, et al. Management of hyperglycaemia in type 2 diabetes mellitus: a consensus algorithm for the initiation and adjustment of therapy. Update regarding the thiazolidinediones. Diabetologia, 2008; 51: 8–11.
10. Laakso M, Cederberg H. Glucose control in diabetes: which target level to aim for? J Intern Med 2012;272:1–12.
11. Schultz RO, Matsuda M, Yee RW, Edelhauser HF, Schultz KJ. Corneal Endothelial Changes in Type I and Type II Diabetes Mellitus. Am J Ophthalmol, 1984; 98: 401–10.
12. McNamara NA, Brand RJ, Polse KA, Bourne WM. Corneal function during normal and high serum glucose levels in diabetes. Invest Ophthalmol Vis Sci., 1998; 39: 3–17.
13. Herse PR. Corneal hydration control in normal and alloxan-induced diabetic rabbits. Invest Ophthalmol Vis Sci., 1990; 31: 2205–13.
14. Lee JS, Oum BS, Choi HY, Lee JE, Cho BM. Differences in corneal thickness and corneal endothelium related to duration in Diabetes. Eye, 2005; 20: 315–8.
15. Busted N, Olsen T, Schmitz O. Clinical observations on the corneal thickness and the corneal endothelium in diabetes mellitus. Br J Ophthalmol, 1981; 65: 687–90.
16. Ravalico G, Tognetto D, Palomba M, Calderini S, Vattovani O. Corneal endothelial function in diabetes: a fluorophotometric study. Ophthalmol J Int Ophtalmol Int J Ophthalmol Z Für Augenheilkd, 1994; 208: 179–84.
17. Keoleian GM, Pach JM, Hodge DO, Trocme SD, Bourne WM. Structural and Functional Studies of the Corneal Endothelium in Diabetes Mellitus. Am J Ophthalmol, 1992; 113: 64–70.
18. Roszkowska AM, Tringali CG, Colosi P, Squeri CA, Ferreri G. Corneal Endothelium Evaluation in Type I and Type II Diabetes mellitus. Ophthalmologica, 1999; 213: 258–61.
19. Inoue K, Kato S, Inoue Y, Amano S, Oshika T. The corneal endothelium and thickness in type II diabetes mellitus. Jpn J Ophthalmol, 2002; 46: 65–9.
20. Wiemer NGM, Dubbelman M, Kostense PJ, Ringens PJ, Polak BCP. The influence of chronic diabetes mellitus on the thickness and the shape of the anterior and posterior surface of the cornea. Cornea, 2007; 26: 1165–70.
21. Su DHW, Wong TY, Wong W-L, Saw S-M, Tan DTH, Shen SY, et al. Diabetes, hyperglycemia, and central corneal thickness: the Singapore Malay Eye Study. Ophthalmology, 2008; 115: 964–8.e1.
22. Yazgan S, Celik U, Kaldırım H, Ayar O, Elbay A, Aykut V, et al. Evaluation of the relationship between corneal biomechanic and HbA1C levels in type 2 diabetes patients. Clin Ophthalmol Auckl NZ, 2014; 8: 1549–53.
23. Oshitari T, Fujimoto N, Hanawa K, Adachi-Usami E, Roy S. Effect of chronic hyperglycemia on

intraocular pressure in patients with diabetes. Am J Ophthalmol, 2007; 143: 363–5.
24. Nemesure B, Wu S-Y, Hennis A, Leske MC, Barbados Eye Studies Group. Factors related to the 4-year risk of high intraocular pressure: the Barbados Eye Studies. Arch Ophthalmol Chic Ill 1960 2003; 121: 856–62.
25. Arora VK, Prasad VN. The intraocular pressure and diabetes--a correlative study. Indian J Ophthalmol 1989; 37: 10–2.
26. Memarzadeh F, Ying-Lai M, Azen SP, Varma R, Los Angeles Latino Eye Study Group. Associations with intraocular pressure in Latinos: the Los Angeles Latino Eye Study. Am J Ophthalmol, 2008; 146: 69–76.
27. Biswas S, Raman R, Koluthungan V, Sharma T. Intraocular pressure and its determinants in subjects with type 2 diabetes mellitus in India. J Prev Med Public Health Yebang Ŭihakhoe Chi., 2011; 44: 157–66.
28. Chihara E. Assessment of true intraocular pressure: the gap between theory and practical data. Surv Ophthalmol, 2008; 53: 203–18.
29. Luce DA. Determining in vivo biomechanical properties of the cornea with an ocular response analyzer. J Cataract Refract Surg, 2005; 31: 156–62.
30. Krueger RR, Ramos-Esteban JC. How might corneal elasticity help us understand diabetes and intraocular pressure? J Refract Surg Thorofare NJ., 1995 2007; 23: 85–8.